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Researchers developing potential coronavirus antibody therapies

Vanderbilt University Medical Center is teaming up with academic, governmental and corporate partners in an unprecedented, fast-tracked global effort to develop antibody-based treatments to protect people exposed to the 2019 novel coronavirus disease, COVID-19.

By: Bill Snyder

Erica Armstrong, research assistant in the Vanderbilt Vaccine Center, pipettes a solution into small tubes of suspended B cells, a first step in the effort to isolate B cells from human serum that produce coronavirus-neutralizing antibodies. (photo by Erin O. Smith)

Dr. Jeff Balser, President and CEO of VUMC, discusses progress on research for antibody-based COVID-19 therapies.

Vanderbilt University Medical Center is teaming up with academic, governmental and corporate partners in an unprecedented, fast-tracked global effort to develop antibody-based treatments to protect people exposed to the 2019 novel coronavirus disease, COVID-19.

Researchers from the Vanderbilt Vaccine Center (VVC) have rapidly responded to this outbreak by building a comprehensive "toolkit" to identify and analyze antibodies isolated from the blood of survivors for their ability to neutralize SARS-CoV-2, the virus that causes COVID-19.

Thousands of antibodies that already have been identified by the VVC are now being analyzed for their ability to inhibit the virus and, more importantly, to prevent it from causing illness. The goal is to develop and manufacture the most promising lead antibodies in preparation for initiating clinical trials to test their efficacy in humans.

"Our goal is to prepare antibodies for human clinical trials by this summer," said James Crowe, MD, director of the Vanderbilt Vaccine Center.

"We have ultra-rapid antibody discovery technologies and already have discovered SARS-CoV-2 antibodies," Crowe said. "Our partners have the manufacturing and product development expertise to turn these antibodies into effective biological drugs very quickly."

VVC researchers have developed techniques for rapidly isolating clones of antibody-producing white blood cells, called "B" cells, which produce antibodies targeting specific viral proteins. In the laboratory, these "monoclonal" antibodies are then comprehensively examined to identify those rare antibodies with a laser-like focus for finding — and neutralizing — a specific virus.

Resources at VUMC that enable the researchers to map antibody sequences and antibody specificities simultaneously and in a high throughput way include the Medical Center's core genomics laboratory, Vanderbilt Technologies for Advanced Genomics (VANTAGE).

Using these techniques, they have generated human monoclonal antibodies against a wide range of pathogenic viruses including Ebola, chikungunya, HIV, dengue, norovirus and respiratory syncytial virus (RSV). They have pioneered the rational design of neutralizing antibody treatments and vaccines, some of which have progressed to clinical trials.

Major funding sources for the VVC include DARPA, the Defense Advanced Research Projects Agency of the U.S. Department of Defense (DoD) and the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health.

The VVC is participating in DARPA's Pandemic Protection Platform (P3) program, a five-year cooperative agreement to develop protective antibody treatments that can be rushed to health care providers within 60 days after the outbreak of viral diseases anywhere in the world.

"Our work over the past several years, through the DARPA Pandemic Prevention Platform (P3), has allowed us to define a flexible and rapid approach algorithm to pursue protective antibodies to almost any viral pathogen," said Robert Carnahan, PhD, VVC associate director.

Last year Carnahan and Crowe led a multi-institutional DARPA "sprint" that developed, in just 11 weeks, a protective antibody-based treatment aimed at stopping the spread of Zika, a mosquito-transmitted virus which can cause severe birth defects in babies whose mothers were infected when they were pregnant.

Vanderbilt's many academic partners in the effort to identify and validate anti-SARS-CoV2 human antibodies include:

- Helen Chu, MD, MPH, assistant professor of Medicine and infectious disease expert at University of Washington School of Medicine in Seattle;
- Michael Diamond, MD, PhD, an internationally known expert on emerging infectious diseases at Washington University School of Medicine in St. Louis;
- Frances Eun-Hyung Lee, MD, director of the Asthma, Allergy, and Immunology Program at Emory University School of Medicine in Atlanta;
- Ralph Baric, PhD, professor of Epidemiology at the University of North Carolina School of Medicine at Chapel Hill; and

- Dan Barouch, MD, PhD, director of the Center for Virology and Vaccine Research at Beth Israel Deaconess Medical Center in Boston.

The following corporate partners also bolster Vanderbilt's research effort.

Berkeley Lights Inc., of Emeryville, California, makes a proprietary cell-selection platform called Beacon that is accelerating the search for neutralizing antibodies against SARS-CoV-2. The platform will be used in other VVC programs to discover antibodies for diverse viruses.

STEMCELL Technologies, Inc., Canada's largest biotechnology company, has partnered with the VVC to develop custom cell-type specific isolation reagents to allow rapid and efficacious isolation of particular B cell subtypes for antibody discovery efforts.

10x Genomics' Chromium Single Cell Immune Profiling Solution is being utilized to rapidly identify matched heavy chain and light chain antibody genes from cells isolated through initial discovery efforts. The company is based in Pleasanton, California.

In collaboration with San Francisco-based Twist Bioscience, antibody gene sequences are synthesized using the company's rapid silicon-based DNA synthesis process. Rapid generation of protein expression constructs from lead antibodies is an essential part of the VVC discovery workflow.

Memphis-based FedEx Corp. is a partner in the critical shipment of non-infectious human donor serum samples to VVC needed for antibody isolation. FedEx Express is using SenseAware to help ensure the safety, logistics, and proper handling of these invaluable samples.

Crowe holds the Ann Scott Carell Chair in the Departments of Pediatrics and Pathology, Microbiology and Immunology in the Vanderbilt University School of Medicine. Carnahan is associate professor of Pediatrics and Radiology and Radiological Sciences.

Others in the VVC who are crucial to the research effort include Pavlo Gilchuk, PhD, senior staff scientist, Seth Zost, PhD, research fellow, Naveen Suryadevara, PhD, staff scientist, Nurgun Kose, senior research specialist, research assistants

Rachel Sutton and Erica Armstrong, lab managers Rachel Nargi and Ryan Irving, and project managers Merissa Mayo and Ginger DeBellis.